Commentary

Chronic kidney disease in India – a hidden epidemic

There is an epidemiological transition taking place in India, with the decline in communicable diseases and a growing burden of chronic disease. In a recent review, Reddy and others noted that 53 per cent of deaths in India in 2005 were due to chronic disease¹. The principal named categories of chronic disease in their report were cardiovascular disease, cancer, chronic respiratory disease and diabetes. Notably, chronic kidney disease (CKD) was not a category on its own merits but most likely included under the ‘other’ category. The World Health Organization laid down certain criteria for a major non-communicable disease (NCD), namely, (i) being a major cause of morbidity and mortality, (ii) being amenable to prevention by community based strategies, and (iii) sharing common risk factors with other NCDs². Though CKD meets these criteria, it does not find a place in this category. There is no reason to suspect that the global epidemic of CKD does not have its counterpart in India and epidemiologic indicators suggest that it is likely to be sizeable. India has been described as the diabetes capital of the world, every fifth diabetic in the world being Indian¹. Hypertension is not far behind – the CURES cohort in Chennai showed that every fifth individual was hypertensive⁴. The increasing prevalence of diabetes, hypertension and associated risk factors such as obesity, hypercholesterolaemia and the metabolic syndrome underscores the potential for sustained and explosive growth of this epidemic. The epidemiology of CKD in India is very different from the West. Patients are roughly two decades younger, and a substantial proportion present with small kidneys, so the aetiology of CKD is unclear⁵. The contribution of less well understood risk factors toward these epidemiologic differences is unknown - low birth weight and relationship to diminished nephron number⁶, variations in Th1/Th2 regulatory lymphocyte balance and relationship to glomerulonephritis as postulated by the ‘Hygiene hypothesis’⁷ and the so called ‘Asian Indian Phenotype’ or ‘Thrifty Phenotype’ of truncal/visceral obesity and insulin resistance⁸, have been poorly studied in this context.

What then is the burden of CKD in India? Recent publications have dealt with mainly single centre reports or regional population based estimates and the definition of CKD has differed. In the absence of nationwide reporting systems or registries, the true incidence and prevalence is difficult to determine. Observational and anecdotal data suggest that the normal ranges of glomerular filtration rate (GFR) may be lower in the predominantly vegetarian, less muscular Indian subjects with different creatinine generation rates, compared to their western counterparts although this issue needs more rigorous study⁹,¹⁰. In the last decade, there has been a major evolution in the definition and classification of CKD that is based upon estimated GFR¹¹. Application of these definitions would impact identification of disease. Therefore issues of global implementation will need to be resolved. Mani¹², working in Chennai, South India, estimated a prevalence of chronic renal failure of 0.16 per cent in the community in 2003; applying the Modification in Diet in Renal Disease (MDRD) equation for GFR estimation in 2005, 0.86 per cent were found to have a GFR <80ml/min/1.73 m²¹³. Agarwal and co-workers¹⁴ arrived at an estimate of 0.78 per cent for CKD, in a community-based sample in New Delhi defined by an elevated serum creatinine >1.8 mg/dl. Estimates for the United States (US) population extrapolated from the National Health and Nutrition Examination Survey (NHANES III) data place the prevalence of CKD stages 4 and 5 (severe decrease in GFR) and CKD stage 3 (moderate decrease in GFR) at 0.4 per cent¹¹. However, such direct comparisons with Western populations are not valid, since the equivalent GFR for a serum creatinine of 1.8 mg/dl in Indians may place the individual anywhere
between CKD stages 2 to 4 depending upon gender and nutritional status. Modi and Jha\textsuperscript{15} reported from an urban population in the city of Bhopal, that the crude and age-adjusted incidence rates of end stage renal disease (ESRD) were 151 and 232 per million population, respectively. ESRD incidence rates lend themselves more easily to international comparisons as the diagnosis is less susceptible to inaccuracies. These estimates are roughly similar to the US\textsuperscript{16}. However, notwithstanding the actual proportions of individuals with disease, the one billion population of India, makes the absolute numbers of patients potentially needing specialized and expensive tertiary care, enormous. Moreover, the socio-economic implications of a young population afflicted with a potentially terminal illness is devastating and in the face of growing epidemics of diabetes and hypertension, the burden of CKD is not likely to ease.

On this background, the study in this issue from the Christian Medical College and Hospital (CMCH) in Vellore, South India\textsuperscript{17}, describing the pre-tertiary care of patients with CKD is timely. Varughese and colleagues studied 561 patients presenting with CKD stage 5 for the first time to their institution, over an eight month period. Advanced CKD was the initial presentation in over half the patients, and CKD was already known in the remainder for a mean duration of a year, possibly less in a majority. Despite more than 90 per cent having been under the care of a nephrologist or internist, the majority were self-referred. Kidney disease related investigations - proteinuria quantification, ultrasonography - had been performed in respectively 48 and 86 per cent, viral screening (hepatitis B, C, HIV) in about a third or less and immunization against hepatitis B initiated in less than a quarter. Blood pressure was inadequately controlled in 62 per cent, 18 per cent were receiving recombinant erythropoietin (rEPO), 40 per cent had already been transfused for the correction of anaemia and about 16 per cent had undergone prior arterio-venous fistula construction. All these parameters, as well as education and preparation for future renal replacement therapy (RRT) were more likely to happen under the care of a nephrologist.

A previous publication from the same centre nearly a decade ago\textsuperscript{18} that studied a cohort of patients beginning haemodialysis (HD), showed a very similar epidemiologic profile, with the mean age in the fourth decade and a similar degree of male preponderance. Diabetic nephropathy and CKD of unknown aetiology were present in 14 and 66 per cent of patients, respectively. The outcome after beginning HD was kidney transplantation in 23 per cent, but 60 per cent discontinued treatment at the centre and were lost to follow up. Roughly a tenth of the original cohort were known to have died and 60 per cent of deaths occurred in the first four weeks of dialysis, a large proportion from complications of severe uremia including pericarditis, pulmonary oedema and severe metabolic acidosis\textsuperscript{5}.

It is evident that there has not been any dramatic evolution of pre-tertiary CKD care or pre-dialysis care in the country. Both the above reports were skewed in favour of the type of patient who had the wherewithal to reach a tertiary referral centre, so these observations are not generalizable and likely overestimate the level of care generally available. Significant barriers exist in the recognition and management of CKD in the country. Socio-economic factors, lack of awareness among patients, a paucity of specific infrastructure and facilities at the community level are all contributory. Notably, we lack a system to measure the quality of care delivered for a given disease. While Varughese and colleagues\textsuperscript{17} showed that blood pressure control was poor in a large proportion of patients with CKD, it is difficult to assess how extensively angiotensin converting enzyme (ACEI) inhibitors may have been used. Although they may be considered standard of care in the West, there is little information about how widely they are used for delaying CKD progression in India. Nearly a fifth were receiving rEPO and a substantial proportion had been transfused. The management of anaemia is especially illustrative as a quality indicator – the treatment - rEPO - is expensive and its suboptimal use to cut costs is likely to be frequent and therefore wasteful. Haemoglobin (Hb) thresholds for rEPO use, adjunctive use of iron supplementation, and appropriate titration of doses are likely conditioned by economic factors. Datta and colleagues\textsuperscript{18} from Chennai, showed the prevalence of anaemia to be 76 per cent among patients with stage 5 CKD; over three quarters had left ventricular hypertrophy. Modi and Jha\textsuperscript{15} reported from incidents dialysis patients between 8.0 and 9.1 g/dl over 2002-2005. Another benchmark of pre-dialysis care is active immunization against hepatitis B. There appears to be a low threshold to correct anaemia by transfusion among pre-dialysis patients and the immune response to hepatitis B vaccination has been consistently poor\textsuperscript{19,20}. Failure to immunize patients with CKD is a missed opportunity to control the risk of liver disease on RRT\textsuperscript{21}. It is well known that the quality of pre-ESRD...
care has a bearing on dialysis outcomes\textsuperscript{22,23}. In the Indian context where dialysis is often abbreviated and kidney transplantation may be either pre-emptive or follow a short period of dialysis, the bearing of pre-dialysis care and management of uremic complications on the outcomes of kidney transplantation is unknown but likely to be significant.

This study\textsuperscript{17} therefore highlights the distance that still needs to be traversed to reach an acceptable level of pre-tertiary CKD care in the country, and the subsequent barriers that exist for adequate pre-ESRD care. Traditionally, preventive strategies in CKD have focused upon tertiary measures. Given the burden of clinical disease in India, such approaches mandate a high level of effectiveness, infrastructure investment, outreach and accessibility to the patient. Awareness of the potential expansion of the CKD epidemic has moved several centres to shift focus to secondary prevention or the detection of asymptomatic clinical disease. The natural history of CKD has a prolonged asymptomatic period during which time substantial loss of kidney function can occur before clinical events become apparent. The individual’s level of awareness of kidney disease in the population is low even in more informed settings\textsuperscript{24}. Once detected, management could incorporate aggressive blood pressure control and blood glucose control for diabetic patients, and the use of ACEI to delay the progression of CKD. The Kidney Help Trust of Chennai, under Dr Mani has run a programme to prevent chronic renal failure by regular screening of an entire population of 25,000 subjects, and treatment of diabetes and hypertension with the cheapest available drugs. This is one of the first grass roots level programmes aimed at prevention. Their total cost amounted to 25 cents per capita of the study population\textsuperscript{13}. Compare this with the cost of RRT at US $ 8000 for kidney transplantation and US $ 5000 for haemodialysis for a year in the face of a per capita income of US $ 430. This community based paradigm should be the other main pillar of a concerted programme to prevent CKD. Many of the past successes with communicable disease eradication (malaria, leprosy, tuberculosis, childhood infections) in public health have succeeded with a community based model of health care delivery.

In 2004, the International Society of Nephrology held a consensus workshop in Hong Kong on the prevention of progression of CKD\textsuperscript{25}. The consensus guidelines covered three key areas – (i) screening for CKD, (ii) evaluation and estimation of the progression of CKD, and (iii) prevention of progression of CKD. All these approaches are best adapted to each community given the variations in genetic make up, dietary, environmental and economic characteristics. In 2005, the Indian Journal of Nephrology used the NKF-KDOQI and European Best Practice Guidelines as a template to compile guidelines for management of CKD and pre-ESRD patients in India. A bi-directional approach is thus needed to establish a continuity of care through the entire spectrum of CKD.

As a tertiary referral centre, the CMCH, Vellore, has pioneered therapy for ESRD in the country and made sterling contributions to the understanding of the epidemiology of kidney disease in the country. It is but fitting that institutions of such caliber now take on the task of optimizing pre-ESRD care, and build the necessary bridges with the community to initiate preventive nephrology programmes.

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